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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,100	04/17/2002	Bernhard Siebold	G-32210A/GBG	6036

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CORPORATE INTELLECTUAL PROPERTY
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EXAMINER	
GHALI, ISIS A D	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 02/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,100	SIEBOLD ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' amendment and request for extension of time, both filed 12/06/2004.

Claims 1-34 have been canceled, and claims 35-54 have been added and included in the prosecution.

The following new ground of rejection is necessitated by applicants' amendment:

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 35-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment of the claims to recite "multi-dosage" has introduced new matter that was not described in the specification as

originally filed. Recourse to specification showed no support to multi-dosage. On the contrary, the original specification disclosed "one dosage unit", original claim 28.

The following rejection were discussed in details in the previous office action, and are maintained for reasons of record:

Claim Rejections - 35 USC § 102

3. Claims 35-51 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 94/03198 ('198).

WO '198 disclosed a stable pharmaceutically acceptable aqueous isotonic formulation containing human growth hormone, buffer solution, non-ionic surfactant, mannitol, preservative and water (abstract; page 3, lines 21-25; page 7, lines 1-8; page 17, claim 12). The amount of human growth hormone is 0.1 to 10 mg/ml (page 5, lines 1-16). The buffered solution included phosphate and present in range of 2 mM to 50 mM (page 6, lines 1-5). The suitable pH ranges from 4-8 (page 6, lines 15-20). The preservatives present in amount of 0.2%-1% and include phenol, benzyl alcohol, meta-cresol, methyl paraben, propyl paraben, benzalconium chloride and benzathonium chloride (page 6, lines 7-13). The non-ionic surfactant includes Pluronic in an amount of 0.1%-1% (w/v) (page 5, lines 27-34; page 16, claim 2). The formulation showed aggregation less than 1% after 18 month when stored at temperature between 2^0C to 25^0C, and the solution was clear to the eye i.e. no crystallization (page 9, lines 8-34; page 10, lines 7-10). The formulation is administered by needleless jet injector gun (page 5, lines 38-39).

Response to Arguments

4. Applicant's arguments filed 12/06/2004 have been fully considered but they are not persuasive. Applicants traverse that anticipatory rejection by arguing that WO '198 disclosed pH 4-8, and the most advantageous pH that is described in the examples is 6.0. Further WO '198 disclosed phosphate buffer among many others but the examples use citrate. WO '198 determines instability from the degradation and/or aggregation of the protein and does not recognize the formation of crystals as a stability issue.

In response to the above argument, the examiner position is that the rejected claims are directed to composition and product, and all the elements of the composition and the product are disclosed by WO '198. The reference disclosed range of pH 4-8 and applicants' claimed range falls within that range, 6.15-6.5. The reference also disclosed the phosphate buffers, as applicants themselves admitted. The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Regarding the reference does not recognized the formation of crystals, the examiner pointing out to the teaching of the reference regarding no aggregation and clarity of the solution that implies the absence of crystals. The word aggregation means "gathering into a mass" and crystallization means "to form definite shape", therefore, the absence of aggregation and clarity of the solution read on absence of crystallization. In any event, the same compositions will inherently have the same physical properties including crystallization.

5. Claims 35-44, 48, 50, 51 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,096,885 ('885).

US '885 disclosed a stable solution comprising human growth hormone, mannitol, buffer, preservative, and nonionic surfactant (abstract; col.2, lines 65-68; col.6, line 25; col.7, lines 1-10, 54-60). The buffer is phosphate buffer (col.5, lines 1-10, 46-47). The pH of the formulation is between 4-8 (col.3, lines 1-3). The amount of surfactant is between 0.1-5% (col.6, lines 40-41). The formulation is administered by jet injector gun (col.6, lines 35-36). The degree of aggregation of a specific compound in a formulation is inherent for the formulation having the same composition. Specific formulation will have the same degree of crystallization under the same conditions.

Response to Arguments

6. Applicant's arguments filed 12/06/2004 have been fully considered but they are not persuasive. Applicants traverse the anticipatory rejection of the claims over US '885 by arguing that US '885 describes a growth hormone formulation containing glycine, while the present invention directed to formulation containing the term "consisting essentially of" and does not contain glycine. Applicants claiming pH 6.15-6.5 which is significantly different from pH 7.4 which was used for all the samples in US '885.

In response to that applicants' argument, the examiner position is that the expression "consisting essentially of" limits the scope of the claim to the specified ingredients, and those that do not materially affect the basic and novel characteristics of the composition. *In re Janakirama-Rao*, 317 F 2d 951, 137 USPQ 893 (CCPA 1963). When applicant contends that modifying components in the reference's composition are

excluded by the recitation of "consisting essentially of", applicant has the burden of showing the basic and novel characteristics of the claimed composition, i.e. showing that the introduction of these components would materially change the characteristics of applicant's composition. *In re De Lajarte,* 337 F 2d 870, 143 USPQ 256 (CCPA 1964). Regarding the pH, the reference disclosed range of pH 4-8 and applicants' claimed range falls within that range, 6.15-6.5. The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

Claim Rejections - 35 USC § 103

7. Claims 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO '198 in view of US 5,334,162 ('162).

The teachings of WO '198 are discussed under 102 rejection above.

However, WO '198 does not teach the kit having the pen injector device and a separate container of the growth hormone as claimed in claims 52-54.

US '162 teaches a cartridge assembly for administration of compounds, wherein the cartridge holds the compound and forms a portion of a pen injector device (abstract). The device is suitable for lyophilized compounds that are moisture and oxygen sensitive such as growth hormone (col.1, lines 42-51).

Thus, it would have been obvious to one having ordinary skill in the art the time of the invention to provide the formulation comprising growth hormone disclosed by WO '198, and administer the formulation by pen injector device comprising the growth

hormone in a cartridge as disclosed by US '162, motivated by the teaching of US '162 that the device is suitable for lyophilized compounds that are moisture and oxygen sensitive such as growth hormone, with reasonable expectation of the having the formulation of WO '198 comprising growth hormone delivered by pen injector device comprising cartridge containing the hormone and deliver it to the needy patient with great success.

Response to Arguments

8. Applicant's arguments filed 12/06/2004 have been fully considered but they are not persuasive. Applicants traverse that obviousness rejection by arguing that WO '198 does not teach the claimed pH, and US '162 does not teach formulation containing growth hormone. The "consisting essentially of" language requires the formulation to be liquid and not lyophilized.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). WO '198 teaches the composition claimed by applicants but does not teach the pen injector device, and US '162 is relied upon for the solely teaching of the pen injector device as a known device for administering pharmaceuticals regardless the type of the pharmaceutical or if it is lyophilized or not. However, the reference disclosed human growth hormone to be delivered by the pen injector, col.1, line 44. WO '198 disclosed range of pH 4-8 and applicants' claimed range falls within that range, 6.15-6.5. The

disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Regarding the expression "consisting essentially of", the expression limits the scope of the claim to the specified ingredients, and those that do not materially affect the basic and novel characteristics of the composition. *In re Janakirama-Rao*, 317 F 2d 951, 137 USPQ 893 (CCPA 1963). When applicant contends that modifying components in the reference's composition are excluded by the recitation of "consisting essentially of", applicant has the burden of showing the basic and novel characteristics of the claimed composition, i.e. showing that the introduction of these components would materially change the characteristics of applicant's composition. *In re De Lajarte,* 337 F 2d 870, 143 USPQ 256 (CCPA 1964). In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

9. Claim 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '885.

The teachings of US '885 are discussed above, however, the reference does not teach the specific preservatives and surfactant as claimed in claim 45-47.

The specific preservatives and non-ionic surfactant claimed in claims 45-47 do not impart patentability to the claims because the prior art recognized the addition of non-ionic surfactant and preservatives to reduce growth hormone aggregation, absent evidence to the contrary.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have a formulation comprising growth hormone and non-ionic surfactant as disclosed by US '885 with the amount of the surfactant less than 0.05%, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller,* 105 USPQ 233.

Response to Arguments

10. Applicant's arguments filed 12/06/2005 have been fully considered but they are not persuasive. Applicants traverse that obviousness rejection by arguing that US '885 describes a growth hormone formulation containing glycine, while the present invention directed to formulation containing the term "consisting essentially of" and does not contain glycine.

In response to that argument, the examiner position is that the expression "consisting essentially of" limits the scope of the claim to the specified ingredients, and those that do not materially affect the basic and novel characteristics of the composition. *In re Janakirama-Rao*, 317 F 2d 951, 137 USPQ 893 (CCPA 1963). When applicant contends that modifying components in the reference's composition are excluded by the recitation of "consisting essentially of", applicant has the burden of showing the basic and novel characteristics of the claimed composition, i.e. showing that the introduction of these components would materially change the characteristics of applicant's composition. *In re De Lajarte,* 337 F 2d 870, 143 USPQ 256 (CCPA 1964).

11. Claims 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '885 in view of US '162.

The teachings of both references are discussed above.

US '885 does not teach the kit and the pen injector device as claimed in claims 52-54.

Thus, it would have been obvious to one having ordinary skill in the art the time of the invention to provide the formulation comprising growth hormone disclosed by US '885, and administer the formulation by pen injector device comprising the growth hormone in a cartridge as disclosed by US '162, motivated by the teaching of US '162 that the device is suitable for lyophilized compounds that are moisture and oxygen sensitive such as growth hormone, with reasonable expectation of the having the formulation of US '885 comprising growth hormone delivered by pen injector device

comprising cartridge containing the hormone and delivers it to the needy patient with great success.

Response to Arguments

12. Applicant's arguments filed 12/06/2004 have been fully considered but they are not persuasive. Applicants traverse that obviousness rejection by arguing that the US '162 does not teach formulation containing growth hormone. Combining US '885 and US '162 does not deliver the present applicants' human growth hormone formulation, as claimed.

In response to that applicants' arguments, US '885 teaches the composition claimed by applicants by does not teach the pen injector device, and US '162 is relied upon for the solely teaching of the pen injector device as a known device for administering pharmaceuticals. However, the reference disclosed human growth hormone to be delivered by the pen injector, col.1, line 44. In response to applicant's argument that combination of the references would not deliver the present formulation, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references

themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one having ordinary skill in the art the time of the invention to provide the formulation comprising growth hormone disclosed by US '885, and administer the formulation by pen injector device comprising the growth hormone in a cartridge as disclosed by US '162, motivated by the teaching of US '162 that the device is suitable for lyophilized compounds that are moisture and oxygen sensitive such as growth hormone, with reasonable expectation of the having the formulation of US '885 comprising growth hormone delivered by pen injector device comprising cartridge containing the hormone and delivers it to the needy patient with great success.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

IG

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